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What is the place of linezolid in the treatment of methicillin-resistant *Staphylococcus aureus* nosocomial pneumonia and complicated skin and soft tissue infections in Europe?

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Methicillin-resistant *Staphylococcus aureus* (MRSA) is a major cause of human morbidity and mortality. MRSA emerged in the early 1960s following the introduction of semi-synthetic, β-lactamase stable penicillins such as methicillin [1]. During the mid-1980s, epidemic strains spread to hospitals throughout the world [2]. For nearly 30 years, MRSA was mainly restricted to hospitals, probably because it had a selective advantage compared with drug-susceptible wild-type *S. aureus* strains.

In the 1990s MRSA was found in the community, in particular in (healthy) individuals who had no direct or indirect link with healthcare settings [3]. Since the beginning of the twenty-first century, community-associated MRSA has been increasing at an alarming rate and has even reached countries that have not had major problems with healthcare-associated MRSA infections, such as Denmark and the Netherlands [4].

For a long time vancomycin has been considered as the standard therapy for serious MRSA infections. However, since 1997 vancomycin use has been challenged by the emergence of MRSA strains with decreased sensitivity to vancomycin [5]. This has prompted the search for novel antibiotics that are efficacious against MRSA.

Linezolid, an oxazolidinone class of antibiotic discovered in the 1990s, was first approved for use in 2000. In Europe, linezolid is indicated to treat nosocomial pneumonia, when known or suspected to be caused by susceptible Gram-positive bacteria; community-acquired pneumonia, when known or suspected to be caused by susceptible Gram-positive bacteria; and complicated skin and soft tissue infections, when microbiological testing has established that the infection is known to be caused by susceptible Gram-positive bacteria.

Since its initial approval, there have been a multitude of microbiological studies, clinical trials and research reports evaluating the effectiveness of linezolid against serious MRSA infections.

From the multiple anti-MRSA drugs that are alternatives to vancomycin, such as clindamycin, trimethoprim-sulfamethoxazole, cyclines, daptomycin, telavancin and ceftaroline [6], the following reviews provide an up-to-date evaluation of the clinical evidence for using linezolid to treat the two main MRSA infections.

For complicated skin and soft tissue infections due to MRSA, linezolid has demonstrated safety, clinical efficacy and favourable outcomes in treatment of these patients. Moreover, with 100% oral bioavailability, the linezolid oral formulation allowed a rapid transition from intravenous to oral therapy and the possibility of an early discharge from the hospital. Therefore, in eligible patients, linezolid reduced the length of hospital stay and overall costs, making this treatment a viable choice for the treatment of MRSA complicated skin and soft tissue infections [7].

For nosocomial pneumonia due to MRSA, the take home message is that vancomycin has remained a standard of care in many European hospitals. However, there is evidence of higher clinical efficacy of linezolid in the treatment of MRSA nosocomial pneumonia in a phase IV, randomized controlled study compared with vancomycin, probably through greater penetration into the epithelial lining fluid of linezolid. Moreover, although overall healthcare resource use may be similar between linezolid and vancomycin, linezolid leads to significantly lower incidence of renal failure than vancomycin, which points to lower healthcare resource costs in linezolid-treated patients [8].

In both indications, resistance to linezolid fortunately remains rare. Most often it is due to a target-site mutation in the 23S rRNA and is associated with prolonged use of linezolid in chronic infections [9]. Recently, emergence of a new mobile linezolid resistance determinant has been reported, which could favour horizontal and interclonal transmission of resistance; it should be closely monitored [10].

Transparency Declaration

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